PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

CORRECTED VERSION

(PCT Article 36 and Rule 70)

CORRECTED IPER

Applicant's or agent's file reference REP07169WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/02976	International filing date *(day/month/year)* 09.07.2003	Priority date *(day/month/year)* 09.07.2002

International Patent Classification (IPC) or both national classification and IPC
G01N33/50

Applicant
CAMBRIDGE UNIVERSITY TECHNICAL SERVICES LTD. et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.02.2004	28.09.2004

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CORRECTED IPER

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/02976

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-13 as originally filed

Claims, Numbers

1-27 as originally filed

Drawings, Sheets

1/6-6/6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does-not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-27
Industrial applicability (IA)	Yes:	Claims	1-27
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item V

Reasoned statement under Art.35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 99 47 922 (MASSACHUSETTS INST. TECHNOL.) 23 September 1999.

   D2: WO 99 67 639 (CALIPER TECHNOLOGIES) 29 December 1999.

2. The subject-matter of claims 1-27 is novel (Art.33(2) PCT). The cited prior art does not disclose a microfluidic device comprising a chamber including a sensor, wherein the chamber surface prevents cell adhesion.

3. The subject-matter of independent claim 1 is not inventive (Art.33(3) PCT).

a. D1 discloses a method for monitoring cells in a microfluidic device, wherein the device comprises a plurality of chambers (wells) connected to sensors for detecting cell properties (page 45, para.3-page 48, para.1; figure 6B). D2 also discloses a microfluidic device comprising channels coated with a material preventing cell adhesion.

b. According to the Applicant, the difference between claim 1 and the prior art including D1 is that cell monitoring is carried out under conditions such that cell adhesion to the microchamber surface is inhibited, wherein the microchamber has a size of the order of magnitude of nl. The technical effect of this difference is inhibition or minimization of biofilm formation in the detection microchamber, thus allowing for size decrease of the detection chamber (page 3, para.3 of the description). The objective technical problem of the present application with respect to the closest prior art is therefore allegedly to adapt the devices of the prior art to a decreased volume of the detection microchamber. The solution proposed is to operate under conditions such that cell adhesion to the microchamber surface is inhibited. An inventive step cannot be acknowledged for claim 1, as the size of the microchamber, which appears to be an essential technical feature of the invention, is not present in the claim. Therefore, the device defined in claim 1 does not solve the technical problem of the application. Furthermore, there is no technical disclosure in the application concerning the

construction and use of microchambers with volumes of the order of magnitude of nl, but only generic statements such as the one already cited above and the one present on page 5, para.4 of the description. This last statement however includes volumes up to 10 microl, i.e. the well volume of ordinary, commercial microtitration plates for ELISA. It would appear, however, that biofilm formation is not critical in said conventional microfluidic devices (see description, page 3 paragraph 3).

3.2. An inventive step cannot be acknowledged also for dependent claim 15, as the volume range defined by the claim includes the well volumes of ordinary, commercial microtitration plates for ELISA.

3.3. The microfluidic device of claim 23 is also not inventive, as the use of an inlet for introducing a liquid into a well appears to be a trivial modification of the device disclosed by D1.

3.4. Dependent claims 2-14, 16-22 and 24-27 do not appear to contain additional features which meet the requirements of inventive step, as all the features of these claims fall within the customary practice of the skilled person or are conventional in the art . In particular, preventing cell adhesion to a surface by coating it with specific materials is well known, see e.g. D1 (page 27, lines 25-31) and D2. D2 discloses the use of polyvinyl alcohol (PVA) as material for inhibiting cell adhesion in a method for monitoring cells in a microfluidic device, wherein the device comprises a plurality of channels connected to sensors for monitoring cell properties or functions (page 21, paragraph 2; page 23, paragraph 2 - page 25, paragraph 2; page 25, paragraph 5 - page 26, paragraph 1; figure 2).

4. The category (entity-claim or method-claim) of claim 1 is not clear (Art.6 PCT). The subject-matter for which protection is sought is not clearly defined, as a method-claim should be defined by the procedural steps necessary to carry out the said method.